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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,247	01/25/2002	Ethan Lerner	10287-066001 / 1791.1	2777
26161	7590	06/16/2004	EXAMINER	
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			KIM, JENNIFER M	
			ART UNIT	PAPER NUMBER
			1617	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/057,247	Applicant(s) LERNER ET AL.	
	Examiner Jennifer Kim	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-5,7-11,18 and 20-22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5,7-11,18,20-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### **Action Summary**

Claims 1, 3-5, 7 and 9-11 of record rejected under 35 U.S.C. 103 (a) over Lerner et al. (WO 98/33379) in view of Zucchetti et al. (U.S. Patent No. 6,037,481) is maintained for the reasons stated in the previous office action.

Claims 2 and 8 of record rejected under 35 U.S.C. 103 (a) over Lerner et al. (WO 98/33379) in view of Yamaguchi et al. (EP 0755671A1) is maintained for the reasons stated in the previous office action.

Claims 18-22 of record rejected under 35 U.S.C. 103 (a) over Lerner et al. (WO 98/33379) in view of Zucchetti et al. (U.S. Patent No. 6,037,481) and further in view of Remington's Pharmaceutical Sciences, 17<sup>th</sup> Edition is maintained for the reasons stated in the previous office action.

### **Response to Arguments**

Applicants' arguments filed on March 22, 2004 have been fully considered but they are not persuasive. Applicants' argue that Lerner teaches treating a subset of conditions associated with aging, i.e. conditions characterized by melanocytes or keratinocytes and neither Lerner nor Zucchetti teach or suggest that wrinkles are in any way associated with unwanted proliferation or insufficient number of melanocytes or

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keratinocytes. This is not persuasive because Learner et al. on page 4, first full paragraph, teach a method of treating a subject for sunburn or other exposure to ultra-violet light or for unwanted effects of aging on the skin by administering a treatment which decreases the level of nitric oxide (NO) in the skin. This teaching would motivate one of ordinary skill in the art to employ an inhibitor of NOS (L-NAME) as taught by Learner to treat any unwanted effects of aging of the skin or other exposure to ultra-violet light to skin. Further, it is well known that wrinkles are unwanted effects of aging of skin as taught by Zucchetti et al. Applicants next argue that wrinkles are not disclosed in Learner and that neither Lerner nor Zucchetti provides any guidance that would lead a person of ordinary skill in the art to decide whether wrinkles are the type of unwanted skin condition that should be treated by decreasing NO levels, or whether wrinkles are the type of unwanted skin condition that should be treated by increasing NO levels. This is not persuasive because Lerner teaches that decreasing the level of nitric oxide by employing L-NAME is useful for the treatment of unwanted effects of aging on the skin and other exposure to ultra-violet light. Therefore, it would have been obvious to one of ordinary skill in the art to employ L-NAME for the treatment of wrinkles well known by Zucchetti et al. as an unwanted skin condition. Applicants argue that Lerner does not teach that all skin conditions accelerated by UV light can be treated with L-NAME. This is not persuasive because Lerner teaches the treatment of skin conditions exposure to ultra-violet light and that wrinkles are the condition results from exposure to ultraviolet rays, UV-B by Yamaguchi et al. One would have been motivated to employ L-NAME for the treatment of wrinkles because L-NAME is effective for the

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treatment of skin conditions exposure to ultra-violet light by Lerner and because wrinkles is a condition results from exposure to ultra-violet light by Yamaguchi et al. Applicants argue that the rejection completely ignores the disclosures in Lerner of conditions that are also accelerated by UV radiation, but which Lerner teaches are treated by increasing NO levels (in contrast to the claimed method, which include administering a NOS inhibitor). This is not persuasive because as addressed earlier, on page 4, first paragraph of Lerner teaches that unwanted effects of aging on the skin and sunburn or other exposure to ultra-violet light can be treated by decreasing nitric oxide level in the skin. One would have been motivated to employ L-NAME for the treatment of wrinkles caused by ultra-violet light because Lerner teach that treatment of unwanted epidermal or dermal conditions comprising exposure to ultra-violet light and wrinkles are the conditions caused by ultra-violet light as well known by Yamaguchi et al. Absent any evidence to contrary, there would have been a reasonable expectation of successfully treating wrinkles caused by exposure to ultra-violet light, with L-NAME to a patient suffering from wrinkles by exposure to ultra-violet light. Applicants argue that Remington does not suggest the use of L-NAME in a method of treating or reducing wrinkles and it does not supply the required motivated to perform a method that includes supplying instructions for using L-NAME to treat wrinkles. This is not persuasive because Remington teaches the labeling instruction to ensure patient understanding of his medication is well known in the art. Therefore, it would have been obvious to one of ordinary skill in the art to incorporate the instruction for the composition taught by Lerner can be used for a skin conditions caused by exposure to

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ultraviolet light (e.g. wrinkles) and can be used for the treating an unwanted effects of the skin aging (e.g. wrinkles) as the condition like wrinkles is well-known to be a condition of an unwanted effects of skin aging and a condition caused by exposure to ultraviolet light. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

In view of the above Office Action of December 17, 2003 is deemed proper and asserted with full force and effect herein to obviate applicants' claims.

### ***Claim Rejections - 35 USC § 103***

Claims 1, 3-5, 7 and 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lerner et al. (WO 98/33379) in view of Zucchetti et al. (U.S. Patent No. 6,037,481).

Lerner et al. teach a topical composition comprising Applicants' NOS inhibitor (e.g. L-NAME) for the treatment of unwanted conditions of skin associated with aging in a subject (a human). (abstract, page 2, lines 16-17, page 9, line 34, page 11, lines 26-38, page 13, lines 26-38, page 7, lines 25-29).

Lerner et al. do not expressly teach the treatment of wrinkle or fine wrinkle, the composition as being sterile and the evaluating the effect of the wrinkles.

Zucchetti et al. teach that the wrinkles are unwanted effects of the skin aging.

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It would have been obvious to one of ordinary skill in the art to modify the Lerner et al.'s method to treat wrinkles or any wrinkle conditions (e.g. fine wrinkles) because Learner et al. teach that composition comprising L-NAME is useful for the unwanted conditions of skin associated with aging and that wrinkles are the unwanted conditions of the skin aging as taught by Zucchetti et al. One would have been motivated to make such a modification in order to achieve expected benefit of reducing unwanted aging conditions of skin (e.g. wrinkles) as taught by Lerner et al. as modified by Zucchetti et al. Absent any evidence to contrary, there would have been a reasonable expectation of successfully treating skin wrinkles with L-NAME. To provide a sterile composition, and the evaluating the effect of medication to determine prognoses (by evaluating the effect of wrinkles) of the disease condition are all deemed obvious since they are all within the knowledge of the skilled artisan and represent conventional technique to manufacturing formulations to avoid contaminants and the routine performance of the physician to treat patients.

Claims 2 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lerner et al. as applied to claims 1, 3-5, 7 and 9-11 above, and further in view of Yamaguchi et al. (EP 0755671A1).

Lerner et al. as applied as before and additional teachings as follow:

Lerner et al. teach that L-NAME is useful for the treatment of sunburn or other exposure to ultra-violet light. (page 4, lines 1-5, page 9, lines 33-35, page 11, line 26-page 12, line 4).

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Lerner et al. do not expressly teach the treatment of wrinkles caused by exposure to UVB radiation.

Yamaguchi et al. disclose that it has been known that the formation of wrinkles is accelerated by exposure to ultraviolet rays, UV-B. (page 2, lines 23-25).

It would have been obvious to one of ordinary skill in the art to employ L-NAME for the treatment of wrinkles caused by ultra-violet light, UV-B because Lerner teach the treatment of unwanted epidermal or dermal conditions comprising exposure to ultra-violet light and wrinkles are the conditions caused by ultra-violet light, UV-B as well-known by Yamaguchi et al. One would have been motivated to make such a modification to achieve expected benefit of treating a disorder caused by exposure to ultra-violet light (e.g. wrinkles) as generally taught by Lerner et al. Absent any evidence to contrary, there would have been a reasonable expectation of successfully treating wrinkles caused by exposure to ultra-violet light, UV-B with L-NAME to a patient suffering from wrinkles by exposure to ultra-violet light.

Claims 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lerner et al. (WO 98/33379) in view of Zucchetti et al. (U.S. Patent No. 6,037,481) as applied to claims 1, 3-5, 7 and 9-11 above, and further in view of Remington's Pharmaceutical Sciences, 17<sup>th</sup> Edition.

The teachings of Lerner et al. and Zucchetti et al. as applied as before and additional teachings of Lerner et al as follows.



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Learner et al. teach that the composition comprising L-NAME can be combined with a non-toxic dermatologically acceptable vehicle or carrier as a cosmetic composition. (page 14, lines 23-29).

Either reference does not teach the instructions for the using the composition to prevent wrinkles.

Remington's Pharmaceutical Sciences teaches that there is an increased awareness that labeling instructions are frequently inadequate to ensure patient understanding of his medication and his adherence or compliance with recommended instruction and that the responsibility that the patient receive specific instructions precautions, and warnings for safe and effective use of prescribed drugs is the shared responsibility of the prescriber and the pharmacist. (page 1792, under Patient Counseling Information).

It would have been obvious to one of ordinary skill in the art to include the instruction for using composition to reduce wrinkles and the directions to apply to the skin prior to sun exposure in Learner et al's composition because Learner's composition is effective for unwanted skin condition associated with aging such as wrinkles and the conditions (wrinkles) caused by exposure to ultraviolet light as taught by Learner as modified by Zucchetti et al. and because there is an increased awareness that labeling instructions are frequently inadequate to ensure patient understanding of his medication and his adherence or compliance with recommended instructions. One would have been motivated to include an instruction with Learner's composition to fulfill the

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responsibility that the patient receive specific instructions precautions, and warnings for safe and effective use of prescribed drugs as the prescriber and the pharmacist.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sreenivasan Padmanabhan  
Supervisory Examiner  
Art Unit 1617

Jmk  
June 7, 2004